

UNITED STATES DISTRICT COURT
SOUTHERN DISTRICT OF NEW YORK

ALLELE BIOTECHNOLOGY AND
PHARMACEUTICALS, INC.,

Plaintiff,

-against-

REGENERON PHARMACEUTICALS, INC.,

Defendant.

CLAIM CONSTRUCTION ORDER

20-CV-08255 (PMH)

PHILIP M. HALPERN, United States District Judge:

This Order sets forth the Court’s patent claim constructions pursuant to *Markman v. Westview Instruments, Inc.*, 517 U.S. 370 (1996). Plaintiff Allele Biotechnology and Pharmaceuticals, Inc. (“Plaintiff” or “Allele”) alleges that Defendant Regeneron Pharmaceuticals, Inc. (“Defendant” or “Regeneron”) infringed its patent for a “Monomeric Yellow-Green Fluorescent Protein from Cephalochordate” (U.S. Patent No. 10,221,221) (Doc. 88-3, the “’221 Patent”). The parties ask the Court to construe four disputed terms: “isolated,” “monomeric or dimeric LanYFP fluorescent protein,” “monomeric polypeptide,” and “non-naturally occurring.” The Court, having thoroughly considered the parties’ briefing (Doc. 87, “Pl. Br.”; Doc. 88, “Campbell Decl.”; Doc. 91, “Def. Br.”; Doc. 93, “Jiminez Decl.”; Doc. 96, “Pl. Reply”; Doc. 99, “Def. Sur-Reply”), and having held a *Markman* hearing on November 21, 2022, herein construes the four disputed terms.

BACKGROUND

I. The ’221 Patent

The ’221 Patent, titled “Monomeric Yellow-Green Fluorescent Protein from Cephalochordate,” addresses the need for bright, monomeric fluorescent proteins. (*See* ’211

Patent). The '221 Patent is directed to novel green/yellow fluorescent proteins derived by protein engineering based on an exemplary wild-type tetrameric yellow fluorescent protein from *Branchiostoma lanceolatum* ("LanYFP"), a marine invertebrate of the cephalochordate subphylum. ('221 Patent at 1-2). The '221 Patent claims a genus of "non-naturally occurring isolated monomeric or dimeric LanYFP fluorescent proteins" and "non-naturally occurring isolated monomeric polypeptides" with stated degrees of sequence identity (*e.g.*, 95%) to mNeonGreen with at least one or at least three of 21 stated mutations. (*Id.* at 22-23).

The specification of the '221 patent contains five claims, set forth below, all of which contain at least one of the disputed terms and are therefore relevant to the instant claim construction:¹

Claim 1: A non-naturally occurring isolated monomeric or dimeric LanYFP fluorescent protein comprising a polypeptide having at least 95% sequence identity to the amino acid sequence of SEQ ID NO: 1, wherein the protein comprises at least one mutation selected from the group consisting of: F15I, R25Q, A45D, Q56H, F67Y, K79V, S100V, F115A, I118K, V140R, T141S, M143K, L144T, D156K, T158S, S163N, Q168R, V171A, N174T, I185Y, and F192Y;

Claim 2: The non-naturally occurring LanYFP fluorescent protein of claim 1, wherein the protein is a monomer;

Claim 3: An isolated non-naturally occurring monomeric polypeptide encoded by a nucleic acid having at least 90% sequence identity to SEQ ID NO: 2 SEQ ID. No. 2, where the nucleotide sequence encodes for a polypeptide which comprises at least one mutation selected from the group consisting of: I118K or N174T, at least one mutation selected from the group consisting of:

¹ "[A] patent claim is that 'portion of the patent document that defines the scope of the patentee's rights.' " *Teva Pharm. USA, Inc. v. Sandoz, Inc.*, 574 U.S. 318, 321 (2015) (quoting *Markman v. Westview Instruments, Inc.*, 517 U.S. 370, 372 (1996)).

V140R, L144T, D156K, T158S, Q168R, and F192Y, and at least one mutation selected from the group consisting of: R25Q, A45D, S163N, F151, Q56H, F67Y, K79V, S100V, F115A, T141S, M143K, V171A, and I185Y;

Claim 4: The non-naturally occurring isolated monomeric or dimeric LanYFP fluorescent protein of claim 1, wherein the protein comprises at least one mutation selected from the group consisting of: I118S and N174T, at least one mutation selected from the group consisting of: V140R, L144T, D156K, T158S, Q168R, and F192Y, and at least one mutation selected from the group consisting of: R25Q, A45D, S163N, F151, Q56H, F67Y, K79V, S100V, F115A, T141S, M143K, V171A, and I185Y; and

Claim 5: The non-naturally occurring isolated monomeric or dimeric LanYFP fluorescent protein of any of claim 1, 3 or 4, wherein the protein comprises a polypeptide having at least 97% sequence identity to the amino acid sequence of SEQ ID NO: 1.

II. Relevant Prosecution History

Before it was ultimately approved, Plaintiff's patent application was rejected by the U.S. Patent Office ("PTO") three separate times: on September 25, 2015, July 8, 2016, and April 11, 2017. (Doc. 88-4, "File History").

A. September 25, 2015 Rejection

The PTO first rejected Plaintiff's application on September 25, 2015, for failure to comply with 35 U.S.C. §§ 101, 102, and 112. (File History at 52-64). The PTO noted that Plaintiff's proposed claims for "an isolated polypeptide set forth in the amino acid of SEQ ID NO:1" were not "markedly different from the product's naturally occurring counterpart" because the specification did not impose any "meaningful limits . . . to set it apart from a natural product." (*Id.* at 58).

Plaintiff responded to the PTO's initial rejection by amending the relevant claims to read "an isolated LanYFP-derived fluorescent protein comprising a polypeptide," which had a stated degree of sequence identity to mNeonGreen. (*Id.* at 68-70). To differentiate its claimed invention from the naturally occurring counterpart, Plaintiff further represented to the PTO that its fluorescent proteins "possess [] functionally superior fluorescent properties" compared to the naturally occurring fluorescent protein, LanYFP. (*Id.* at 71-72).

B. July 8, 2016 Rejection

The PTO rejected Plaintiff's application for a second time on July 8, 2016. Despite Plaintiff's amendments, the patent examiner stated that "[t]he fact pattern in the application is that the claims are directed to a product that initially appears non-naturally occurring, however is a natural product." (File History at 78). The examiner went on to note that a claimed invention which only shares a degree of identity (*e.g.*, 92% of sequence identity) is "simply truncating the native structure" instead of altering it and therefore not patent-eligible. (*Id.* at 79).

Plaintiff responded to this second rejection by adding the phrase "non-naturally occurring" to the relevant claims. (*Id.* at 88). Plaintiff further represented that the claimed invention, monomeric or dimeric fluorescent proteins, were different from the naturally occurring counterpart, because that protein only "occurs as a tetramer in nature." (*Id.* at 91). Plaintiff further stated that the claimed invention contained "significant sequence differences" from the naturally occurring counterpart as a result of 21 stated mutations. (*Id.*).

C. April 11, 2017 Rejection

The PTO rejected Plaintiff's application for a third time on April 11, 2017. The patent examiner considered Plaintiff's argument that the claimed invention was different than the naturally occurring counterpart because the monomeric and dimeric embodiments of the

fluorescent proteins did not occur in nature. (File History at 102). However, the examiner stated that Plaintiff's arguments imposed "limitations not present in the instant claims." (*Id.*). Put another way, while it may be true that the monomeric and dimeric forms of the fluorescent protein did not occur in nature, the language of the claims themselves did not reflect this limitation and, therefore, the claimed invention still included a natural phenomenon in violation of 35 U.S.C. § 101.

Plaintiff responded to this third rejection by amending the claims to their current, approved forms. (*Id.* at 108-109). The amended claims added the language describing the fluorescent protein as "monomeric or dimeric" and specifying that the nucleic acid comprises at least 1 out of 21 stated mutations. (*Id.*). The PTO subsequently issued the patent on March 5, 2019. (*Id.* at 148).

STANDARD OF REVIEW

The Court's role at this stage in a patent proceeding is to determine, when necessary and appropriate, the meaning of terms within a claim in order to assist the fact finder in making subsequent and ultimate decisions as to whether a patent has in fact been infringed. The purpose of claim construction is to define terms so that a jury may be properly instructed. *See Sulzer Textil A.G. v. Picanol N.V.*, 358 F.3d 1356, 1366 (Fed. Cir. 2004) ("the trial court in a patent case must at minimum take steps to assure that the jury understands that it is not free to consider its own meanings for disputed claim terms and that the district court's claim construction . . . is adopted and applied by the jury in its deliberation of the facts"). The Court's determination of disputed factual issues is often necessary to the determination of the appropriate construction of a term. *See Markman v. Westview Instruments, Inc.*, 517 U.S. 370, 389 (1996) ("[t]he construction of written instruments is one of those things that judges often do and are likely to do better than jurors unburdened by training in exegesis"). Claim construction is an issue of law properly decided by the Court, and the analysis is substantially guided by the Federal Circuit's decisions in *Phillips v.*

AWH Corp., 415 F.3d 1303 (Fed. Cir. 2005) (en banc), and *Markman v. Westview Instruments, Inc.*, 52 F.3d 967 (Fed. Cir. 1995) (en banc).

Claim terms are to be given the meaning understood by a person of ordinary skill in the art at the time of invention. *Phillips*, 415 F.3d at 1313. “Properly viewed, the ‘ordinary meaning’ of a claim term is its meaning to the ordinary artisan after reading the entire patent.” *Id.* at 1321. When interpreting the meaning of claim terms, “words of a claim are generally given their ordinary and customary meaning” as understood by “a person of ordinary skill in the art at the time of invention, *i.e.*, as of the effective filing date of the patent application.”² *Id.* at 1312–13. Courts must read a claim term “not only in the context of the particular claim in which the disputed term appears, but in the context of the entire patent, including the specification.” *Id.* at 1313. “It is a bedrock principle of patent law that the claims of a patent define the invention to which the patentee is entitled the right to exclude.” *Id.* at 1312.

The Federal Circuit has emphasized the importance of intrinsic evidence in claim construction: the words of the claim themselves, the written description in the patent’s specification, and, when necessary, the history of the patent application’s prosecution before the PTO. *Seabed Geosolutions (US) Inc. v. Magseis FF LLC*, 8 F.4th 1285, 1287 (Fed. Cir. 2021) (“we still give primacy to intrinsic evidence, and we resort to extrinsic evidence to construe claims only if it consistent with intrinsic evidence”); *see also Phillips*, 415 F.3d at 1318 (“[A] court should discount any expert testimony that is clearly at odds with the claim construction mandated by the claims themselves, the written description, and the prosecution history.”).

² The parties agree that “a person of ordinary skill in the art at the time of invention” would have a Ph.D or equivalent degree in biochemistry, chemistry, or a related discipline and two or more years of experience in fluorescent protein engineering. (*See* Doc. 87 at 9; Doc. 91 at 12).

Claim language must also be read in the context of the specification. *Id.* at 1315. The specification “is always highly relevant to the claim construction analysis. Usually it is dispositive; it is the single best guide to the meaning of a disputed term.” *Id.* (quoting *Vitronics Corp. v. Conceptronic, Inc.*, 90 F.3d 1576, 1582 (Fed. Cir. 1996)). The specification also acts as a dictionary “when it defines terms by implication.” *Vitronics*, 90 F.3d at 1582. However, when relying on the specification to interpret claim terms, a court should not be confined to the embodiments described in the specification. *Phillips*, 415 F.3d at 1323. The mistake of “reading a limitation from the written description into the claims” is “one of the cardinal sins of patent law.” *Id.* at 1320 (quoting *SciMed Life Sys., Inc. v. Advanced Cardiovascular Sys., Inc.*, 242 F.3d 1337, 1340 (Fed. Cir. 2001)).

“In addition to consulting the specification, [the Federal Circuit has] held that a court should also consider the patent’s prosecution history, if it is in evidence.” *Id.* at 1317. The prosecution history “can often inform the meaning of the claim language by demonstrating how the inventor understood the invention and whether the inventor limited the invention in the course of prosecution, making the claim scope narrower than it would otherwise be.” *Id.* at 1317. However, “because the prosecution history represents an ongoing negotiation between the PTO and the applicant, rather than the final product of that negotiation, it often lacks the clarity of the specification and thus is less useful for claim construction purposes.” *Id.*

Courts may also rely on “extrinsic” evidence such as dictionaries, learned treatises, and expert testimony, which may serve as a source of “accepted meanings of terms used in various fields of science and technology” or provide “background on the technology at issue.” *Id.* at 1317–18. However, such extrinsic evidence is “less significant than the intrinsic record in determining

the legally operative meaning of claim language,” and should only be considered within the context of the intrinsic evidence. *Id.* at 1317-19.

The process of claim construction begins with the language of the claims themselves, which the patentee selected to “particularly point out and distinctly claim the subject matter which the applicant regards as his invention.” *Phillips*, at 1311-12 (quoting 35 U.S.C. § 112). Thus, “the claims themselves provide substantial guidance as to the meaning of particular claim terms.” *Id.* at 1314. In addition to the particular claim being examined, the context provided by other claims may be helpful as well. *Id.*

A party seeking to limit the scope of a patent or else invalidate it altogether may do so, *inter alia*, by arguing that a claim term is indefinite or that the patentee disavowed the full scope of a term during representations made during prosecution of the patent application. “[A]n inventor may disavow claims lacking a particular feature when the specification describes ‘the present invention’ as having that feature.” *Poly-Am., L.P. v. API Indus., Inc.*, 839 F.3d 1131, 1138 (Fed. Cir. 2016). A party seeking to prove that a patentee disclaimed claim scope must be able to show that the patentee evinced a “clear and unmistakable surrender of claim scope.” *Aylus Networks, Inc. v. Apple Inc.*, 856 F.3d 1353, 1362 (Fed. Cir. 2017). The standard for finding disavowal are “exacting” as “the specification or prosecution history [must] make clear that the invention does not include a particular feature.” *GE Lighting Sols., LLC v. AgiLight, Inc.*, 750 F.3d 1304, 1309 (Fed. Cir. 2014).

Another avenue for limiting the scope of a patent, or invalidating one entirely, is through the definiteness requirement imposed by 35 U.S.C. § 112. If a term is indefinite, then the claims in which it appears are invalid. *See Synchronoss Techs., Inc. v. Dropbox, Inc.*, 987 F.3d 1358, 1368 (Fed. Cir. 2021). Definiteness is determined from the point of view of a person of ordinary skill in

the art at the time of filing and is resolved with reference to the patent’s specification and prosecution history. *Nautilus, Inc. v. Biosig Instruments, Inc.*, 572 U.S. 898, 908 (2014). “The definiteness requirement, so understood, mandates clarity, while recognizing that absolute precision is unattainable.” *Nautilus*, 572 U.S. at 910. Instead, “the certainty which the law requires in patents is not greater than is reasonable, having regard to their subject-matter.” *Id.* Finally, indefiniteness must be proven by “clear and convincing evidence” because patents are entitled to a presumption of validity that is not readily overcome. *VR Optics, LLC v. Peloton Interactive, Inc.*, 345 F. Supp. 3d 394, 398 (S.D.N.Y. 2018) (citing *BASF Corp. v. Johnson Matthey Inc.*, 875 F.3d 1360, 1365 (Fed. Cir. 2017)).³

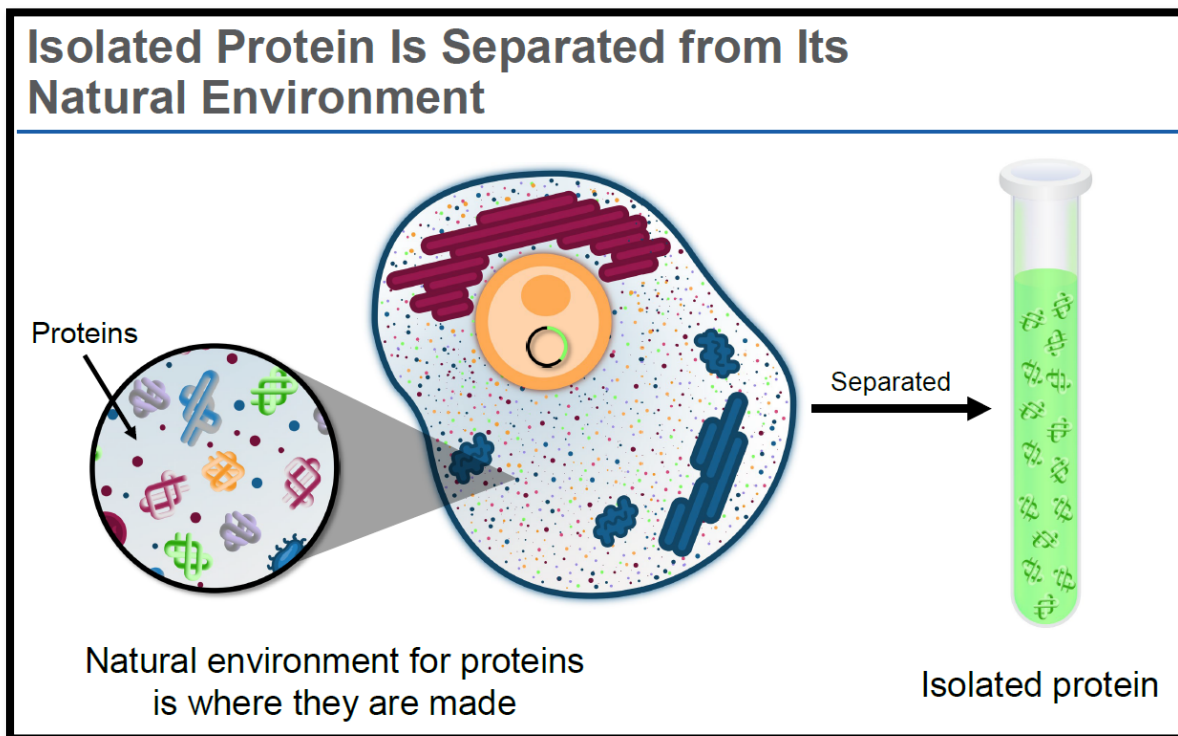
ANALYSIS

I. “Isolated” (Claims 1, 3, 4, and 5)

Allele’s Proposed Construction	Regeneron’s Proposed Construction
The protein is present in other than its natural environment.	The protein is separated from its natural environment.

The primary dispute here is whether the term “isolated” requires that the fluorescent protein be affirmatively separated from the cell in which it was expressed. Regeneron argues that because some of the examples in the specification feature the fluorescent protein separated from its cell, the term “isolated” must require such affirmative separation. (Def. Br. at 13-15). Regeneron, in support of its proposed construction, offered the following illustration during the *Markman* hearing held by the Court:

³ This clear and convincing burden of proof standard associated with the definiteness analysis is “one of the few instances where there is a burden of proof in *Markman* proceedings.” Peter S. Menell et. al., *Patent Claim Construction: A Modern Synthesis and Structured Framework*, 25 Berkeley Tech. L.J. 711, 768 (2010).



(11/21/2022 *Markman* Hearing, Defendant's Presentation at 7).

Defendant further argues that the prosecution history reflects that the examiner understood the term “isolated” to mean separated because the examiner stated that an isolated protein “can be made by . . . synthetic peptide synthesis or purification from the natural source.” (*Id.* at 16). Allele argues that the specification is replete with embodiments that describe fluorescent proteins not separated from the cell in which they were expressed, or purified, as part of the invention. (Pl. Reply at 4-5 (citing the '221 Patent at 8-11)). Allele further argues that statements made by the examiner, not Allele, during the prosecution history cannot serve as evidence to limit the term as Regeneron proposes. (*Id.* at 6).

Regeneron's proposed construction excludes, without any explanation, several embodiments that describe fluorescent proteins not separated from the cell in which they were expressed. ('221 Patent at 8-11). Regeneron's proposed construction also ignores the '221 Patent's

abstract, which expressly contemplates “a host cell comprising the vector, and the use of the vector in a method for expressing the nucleic acid sequence.” (*Id.* at 2). As the Federal Circuit instructed in *Oatey Co. v. IPS Corp.*, “where claims can reasonably [be] interpreted to include a specific embodiment, it is incorrect to construe the claims to exclude that embodiment, absent probative evidence [to] the contrary.” 514 F.3d 1271, 1277 (Fed. Cir. 2008). Here, Regeneron has not presented probative evidence sufficient to support its proposed construction. That the patent examiner stated that a protein could theoretically be purified is not probative to whether the term “isolated” requires the affirmative step of separation of the fluorescent protein from the cell.

Accordingly, the Court construes “isolated” in the context used in Claims 1, 3, 4, and 5 as meaning “the protein is present in other than its natural environment.”

II. “Monomeric or dimeric LanYFP fluorescent protein” (Claims 1, 4, and 5) and “monomeric polypeptide” (Claim 3)

	Allele’s Proposed Construction	Regeneron’s Proposed Construction
Monomeric or dimeric LanYFP fluorescent protein	No construction needed (plain and ordinary meaning).	Monomeric or dimeric green/yellow fluorescent protein that has improved extinction coefficient, quantum yield, and brightness compared to mCitrine.
Monomeric polypeptide	No construction needed (plain and ordinary meaning).	Monomeric polypeptide that has improved extinction coefficient, quantum yield, and brightness compared to mCitrine

Plaintiff argues that these two terms should be assigned their plain and ordinary meaning. (Pl. Br. at 17-19). Defendant does not argue that the plain and ordinary meaning of these two terms is disputed, nor does Defendant argue that these terms are ambiguous in any way. (Def. Br. at 20-

22). Rather, Defendant argues that the Court should read limitations into these claims because Plaintiff disavowed the full scope of the plain and ordinary meaning. (*Id.*). Defendant, in support of this argument, points to three statements Plaintiff made to the examiner over the course of a four-year period regarding the properties of the claimed invention (*Id.* at 21) as follows:

- “Claims 3 and 5 as a whole are directed to embodiments of fluorescent proteins (FPs) derived/generated from a cephalochordate *Branchiostoma lanceolatum* protein, which occurs as a tetramer in nature. These exemplary monomeric or dimeric embodiments of the proteins disclosed herein were designed and generated by structure and docking algorithms using protein engineering techniques and have no known structural or homologs in nature and possess superior functionally superior fluorescent properties.” (File History at 72);
- “Applicants respectfully disagree with the Examiner’s assertion that the ‘claimed invention encompasses products that have characteristics that are not markedly different from the product’s naturally occurring counterpart in its natural state’ because inherent in the recited sequence (SEQ ID NO: 2) is a structure significantly different than the structure of the wild-type protein found in nature. Applicants respectfully note that each of the present claims requires the polypeptide to be in a monomeric or dimeric form, which results from the claimed sequences and is not a form exhibited by the naturally occurring wild-type protein. The exemplary monomers and dimers described in the instant application were specially engineered based on the inventors’ insights, to adopt a monomeric or dimeric form with enhanced or retained fluorescent properties. The instant application further describes the superior properties of exemplary polypeptides of this invention, including a brighter fluorescent signal; improved use as fluorescent tags due to the superior properties of the smaller, monomeric or dimeric form; and superior photostability. Each of the present claims requires a monomeric or dimeric form which requires an engineered change to achieve that property.” (*Id.* at 112);
- “Furthermore, the exemplary protein (mNeonGreen) is the brightest monomeric GFP labeling fluorescent protein [] in the market today—mNeonGreen exhibits a brightness of 274% compared to that of EGFP, whereas the commercially available mCitrine exhibits a brightness of only 174%. One of ordinary skill in the art would appreciate that in general, monomers are not as bright as dimers or tetramers, because there are fewer emissive entities. While the brightness, quantum yields, and extinction coefficients decrease from tetrameric LanYFP to dimeric dLanYFP to monomeric mNeonGreen, the brightness per monomeric unit is the highest for the exemplary protein mNeonGreen (Table 1). In addition, mNeonGreen exhibits a pKa of 5.7, which as noted in the specification is ‘similar to most modern GFPs and YFPs’ (present specification, ¶[0030]). In contrast, the tetrameric LanYFP exhibits a pKa of 3.5. Thus, the exemplary monomeric protein mNeonGreen exhibits

markedly different physical differences from the naturally occurring tetrameric LanYFP protein.” (*Id.* at 113).⁴

As an initial matter, where, as here, the plain and ordinary meaning of a term is undisputed, a district court may properly decline to construe such a claim. *ActiveVideo Networks, Inc. v. Verizon Commc’ns, Inc.*, 694 F.3d 1312, 1326 (Fed. Cir. 2012) (holding that a district court “did not err in concluding that these terms have plain meanings that do not require additional construction” and further noting that it would be erroneous to “read[] limitations” into such undisputed claims).

Regardless, Defendant has failed to show that Plaintiff disavowed the full scope of the plain and ordinary meaning of these terms. Each of the three statements cited by Defendants in support of this argument were made in response to the examiner’s rejection under 35 U.S.C. § 101 for ineligible subject matter. (File History at 39, 72, 90-91, 112). These statements were made as part of a broader discussion between the examiner and Plaintiff on whether the patent sufficiently distinguished the claimed invention from its naturally occurring counterpart. (*Id.*). Plaintiff, in each of the three statements, expressly distinguished its claimed invention from the naturally occurring tetrameric LanYFP protein. (*See supra* at 11-12). Plaintiff did not claim, as Defendant suggests, that the claimed invention has superior fluorescent properties over the prior art. (*Id.*). These three statements are insufficient to show that Plaintiff disavowed any scope for the plain and ordinary meanings of these two terms. *Cadence Pharms. Inc. v. Exela PharmSci Inc.*, 780 F.3d 1364, 1369 (Fed. Cir. 2015) (declining to impose a limitation on a term from statements made by the patent-holder during prosecution in response to a rejection).

⁴ Defendant also cites to Table 1 in the ’221 Patent, which compares *Branchiostoma lanceolatum*-derived fluorescent proteins to other green and yellow fluorescent proteins, in support of its proposed construction for these terms. (Def. Br. at 19, 21).

Accordingly, the Court declines to construe the terms “monomeric dimeric LanYFP fluorescent protein” and “monomeric polypeptide” because the parties agree that each term’s plain and ordinary meaning is not in dispute, and in any event Regeneron has not satisfied its burden of proof that the Court should impose limitations into these terms.

III. “Non-Naturally Occurring” (Claims 1-5)

Allele’s Proposed Construction	Regeneron’s Proposed Construction
Different in amino acid sequence from a yellow/green fluorescent protein of the species <i>Branchiostoma lanceolatum</i> that is found “as is” in nature	Indefinite.

Plaintiff argues that the term “non-naturally occurring” should be construed to mean “different in amino acid sequence from a yellow/green fluorescent protein of the species *Branchiostoma lanceolatum* that is found ‘as is’ in nature.” (Pl. Br. at 10-12). Defendant argues that this term is indefinite because no person of ordinary skill in the art can be certain if a fluorescent protein is not found in nature because new naturally occurring proteins are still being discovered. (Def. Br. at 22-25).

Defendant, however, has failed to meet its burden to prove by clear and convincing evidence that this term is indefinite. The existence of undiscovered naturally occurring fluorescent proteins does not render the term indefinite. The parties agree that a person of ordinary skill in the art would be able to determine whether a protein is naturally occurring by comparing that sequence to a widely used database maintained by the National Institutes of Health known as “GenBank.” (See Def. Br. at 23; Pl. Reply at 2). Referring to GenBank and other available databases, a person of reasonable skill would, conversely, be able to determine within a reasonable degree of certainty

that a fluorescent protein is *not* naturally occurring. This is sufficient, as “some modicum of uncertainty” is allowed in assessing a term’s definiteness. *Nautilus*, 572 U.S. at 899.

Further, the specification itself provides critical context that confirms Plaintiff’s proposed construction of the term. For example, the specification states: “[t]he present disclosure provides novel green/yellow fluorescent proteins derived by protein engineering based on exemplary yellow fluorescent proteins from *Branchiostoma lanceolatum* (LanYFP...).” (The ’221 Patent at 61-63). This language supports Plaintiff’s proposed construction in describing how protein engineering techniques were used to arrive at the claimed fluorescent proteins that differ from those found “as is” in nature.

The prosecution history is in accord with Plaintiff’s proposed construction as well. Plaintiff amended its claims to include the term “non-naturally occurring” in response to the PTO’s rejection of its application for not distinguishing the claimed invention from its naturally occurring counterpart. (File History at 90-92). In addition to adding the term, Plaintiff represented that the claimed invention, monomeric or dimeric fluorescent proteins, were different from the naturally occurring counterpart, LanYFP, which “occurs as a tetramer.” (*Id.* at 91). Plaintiff further stated that the claimed invention contained “significant sequence differences” from the naturally occurring counterpart as a result of 21 stated mutations. (*Id.*). This amendment was made specifically in response to the examiner asking Plaintiff to clarify how its claimed invention was different than its naturally occurring counterpart. Through the addition of the term “non-naturally occurring,” Plaintiff communicated to the examiner that the amino acid sequence of the claimed invention was different from the protein that is found “as is” in nature. That is precisely the construction Plaintiff now asks the Court to adopt.

Accordingly, the Court construes “non-naturally occurring” in the context used in claims 1-5 as meaning “different in amino acid sequence from a yellow/green fluorescent protein of the species *Branchiostoma lanceolatum* that is found ‘as is’ in nature.”

CONCLUSION

For the foregoing reasons, the Court construes the disputed terms as set forth hereinabove.

SO ORDERED.

Dated: White Plains, New York
December 5, 2022



PHILIP M. HALPERN
United States District Judge